

THE MEASUREMENT OF BLOOD VESSELS IN RETINAL PHOTOGRAPHS
OF SUBMARINERS

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SUMMARY PAGE

THE PROBLEM

To devise a technique for assessing the general health of the vascular system of submariners from photographs of their retinas.

FINDINGS

Measures are made of the diameters of retinal arteries and veins (A/V ratios) on photographs by using a microscope with a micrometer attachment. Photographs of 40 eyes were evaluated independently by two measurers. The A/V ratios are comparable to those found in the literature and the inter-measurer reliability is good.

APPLICATION

The measurements of retinal vessels will be made periodically on men as part of the longitudinal health study of submariners. These data will be correlated with blood pressures and various other aspects of the men's medical and service history to ascertain effects of continuous exposure to submarine and diving environments.

ADMINISTRATIVE INFORMATION

The investigation was conducted as a part of Bureau of Medicine and Surgery Research Work Unit M4306.01-4020B, Longitudinal Health Study of Personnel Exposed to Submarine Environment and Diving Hazards for Extended Periods. The present report is No. 2 on that Work Unit. It was approved for publication on 23 Mar 1970 and designated as Submarine Medical Research Laboratory Report No. 617.

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ABSTRACT

The literature describing the relationship between retinal blood vessels and general vascular disease is reviewed. Data on the differences in caliber of arteries to veins (A/V ratios) among normal and hypertensive subjects is summarized. The specific problems that arise in attempting to evaluate A/V ratios in different individuals are discussed and a standardized technique for measuring retinal photographs is described which overcomes various difficulties common to A/V measurements. Sample data using the technique are given.

1. The first part of the paper discusses the importance of the study of the history of the United States. It is argued that the study of the history of the United States is essential for a full understanding of the country and its people. The paper then discusses the various methods used by historians to study the past, including the use of primary and secondary sources, and the importance of critical thinking in the study of history.

THE MEASUREMENT OF BLOOD VESSELS IN RETINAL PHOTOGRAPHS OF SUBMARINERS

INTRODUCTION

An ongoing investigation at the Submarine Medical Research Laboratory is the longitudinal study of the health and personality changes of men exposed for long periods of time to submarine environments. A battery of tests designed to measure visual performance and ocular health is included in the study. One of these--fundus photographs of the men's eyes--was selected to provide a permanent record of retinal vascular structure available for comparison with photographs taken in the future and with other indices of general health.

Examination of the retina has become an important diagnostic tool in the study of vascular disease. Because of the close relationship between the retinal blood vessels and those of the brain, study of the retinal vessels offers a unique opportunity for prediction of the condition of cerebral vessels.

A large number of retinal symptoms of vascular disease have been enumerated over the years. Duke-Elder¹ classifies three major signs: (1) changes occurring at the arteriovenous crossings, usually called A-V nicking; (2) narrowing of isolated sectors of arteriolar wall; and (3) generalized attenuation and straightening of the retinal arterioles. He also cites a number of minor signs such as decreased translucency of vessel walls, changes in the vascular reflex, increased tortuosity, hemorrhages and exudates.

Most authors agree that the importance of retinal examination cannot be overestimated. For example, Shelburne² says that it is the single most important examination of the patient with sustained hypertension. Tagamlik³ states that the results of the investigation of 171 hypertensive patients showed changes in the optic fundus to be among the more important signs for the diagnosis and prognosis of the disease. The earliest and most constant sign of hypertension was the vascular changes. Minsky's summary is equally emphatic:

"It is well known that during the course of hypertension remissions in blood pressure figures occur. During the periods of exacerbation, on the other hand, there take place such profound, irreversible changes in the appearance of the retinal vessels, particularly the arterioles, that they remain as permanent signs, to be read by him who will. So true is this that, although intercurrent coronary thrombosis will markedly lower the sphygmomanometer readings, it will alter not at all the retinal vessel changes developed during the high diastolic levels that were reached previously. Once a persistently elevated diastolic pressure has existed, there will always remain a telltale picture in the vessels of the fundus." (Minsky⁴, p.863)

Despite the importance attached to ophthalmoscopic examination in vascular disease and the repeated reference to irreversible changes in retinal arterioles, the significance of one of Duke-Elder's three major symptoms--the attenuation of the retinal arterioles--has been repeatedly attacked.

Attenuation implies, of course, the existence of some standard by which the reduction in size may be judged; ideally this standard should be the size of the same vessel before the attenuation. Since this poses a practical impossibility

in most cases, comparison with venous diameters is the common technique.

It is well established that the retinal arteries are smaller on the average than the veins, by a factor of 2:3 or 3:4. A small ratio of arteriole to venule diameters (A/V), generally of .5 or less, thus becomes a symptom of vascular disease. The evaluation is usually made during a routine ophthalmoscopic examination; it is thus a visual estimate by the physician of the average size of arteries to that of veins.

Obviously, not any arteriole can be compared with any venule, since the diameters of both vary in different branches of the vessels. The refined technique thus is to estimate the size of pairs of vessels of comparable order of division; for example, the third branch of the superior temporal artery is compared with the third branch of the superior temporal vein.

This technique, the estimation of A/V ratios, has born the brunt of the attack and with it, by implication, the use of arteriole attenuation as a symptom of retinal disease. Two examples of the type of criticism levelled against the A/V ratio are given below:

"The low incidence of significantly reduced A/V ratios in hypertensive patients, the poor correlation between the magnitude of the ratio and the severity of the disease and the relatively large error in estimating the ratio in individual cases all combine to make the assessment of generalized retinal arteriolar narrowing of little value in determining prognosis in essential hypertension." (Nicholls et al,⁵ p.44)

and

"The arteriovenous ratio is obviously useless as a guide to arteriolar calibre unless two vessels of a comparable order of division are selected, but it has

been shown that this is difficult, tedious, and often impossible by casual ophthalmoscopy, or even by retinal photography." (Stokoe and Turner,⁶ p. 39)

On the other hand, examination of the data available in the literature reveals average differences in A/V ratio which are consistently smaller for groups of individuals with vascular disease than for groups of normal individuals.^{5,7} For example, the data published by Nicholls, Turnbull and Evelyn on three groups of 100 subjects are shown in Table I to indicate the size of the differences that may be expected. The differences between normals and hypertensives are small and the distributions show considerable overlap; nonetheless, the differences are obviously real and highly significant.*

Table I. Average A/V Ratios on Three Groups of Subjects (from Nicholls, Turnbull & Evelyn⁵)

Group	Mean	Range
100 Normals	.75	.60 - .98
100 Normals	.77	.55 - 1.00
100 Hypertensives	.64	.33 - .87

*Nicholls et al⁵ do not report standard deviations but give instead the entire range of A/V ratios for each of the groups. However, even using the range as the best estimate of variability (a procedure which grossly overestimates the amount of variability), the differences between normals and hypertensives are significant at better than the .01 level.

The skepticism of many ophthalmologists concerning the use of A/V ratios can be accounted for on several grounds. First, the differences in caliber of arteries and veins are admittedly small and the usual technique of visually estimating the ratio size to the nearest tenth is grossly inadequate. It is well known to students of perception that an absolute judgment to .10 of two, non-contiguous sizes is beyond the capability of most human observers.⁸ Other techniques, such as measurement of retinal photographs, are required.

Second, practicing physicians may be influenced by the fact that the fundus in question belongs to a hypertensive patient and unconsciously underestimate the ratio. Thus, claims for large differences in A/V ratios between normals and patients may be made, claims which cannot be substantiated by careful research. A number of investigators are well aware of this danger; Shelburne, for example, still forces himself to describe his ophthalmoscopic findings to his students before he obtains any data on the patient's blood pressure.^{2, p.13}

Third is the difficulty of finding comparable vessels in some subjects. This has been carefully documented by Stokoe and Turner⁶ in a study of retinal photographs. For example, they state that in a random selection of 80 fundus pictures, comparable vessels could not be found in any quadrant in 10 of the pictures. For these ten, then, the technique of estimating A/V ratios, as commonly employed, is useless.

Finally, A/V ratios are distributed normally in the populations of normals

and of patients and the two distributions overlap considerably. Differences thus apply only to averages and no prognosis can be made with certainty for individual cases. This reduces the usefulness of the technique to the clinical ophthalmologist and he may discount it entirely because of patients that have both "normal" ratios and severe hypertension.

Thus we may conclude that the method of assessing A/V ratios as commonly employed by clinical ophthalmologists is fraught with difficulties and the physicians' skepticism is well-founded in many cases. Nonetheless, reliable differences in A/V ratios among normals and patients do exist and none of the difficulties are insurmountable. Reliable techniques of measuring vessels on fundus photographs can be developed; measures can be made by individuals with no prior knowledge concerning the owner of the fundus; substitutes for comparable vessels can be selected; and prognosis for groups of individuals should be excellent. While the care that is necessary to develop and use these techniques may be unrealistic for the clinical ophthalmologist, the rewards in terms of research should be immense.

The purpose of this paper, therefore, is to describe a technique devised for measuring A/V ratios in a group of submariners and to report preliminary results on its reliability.

PHOTOGRAPHIC AND MEASUREMENT PROCEDURES

The subject's pupil is dilated with Mydracil (.005) and three fundus

photographs in color are taken with a Zeiss Ikon Fundus camera. Care is taken in the positioning of the camera to obtain a view of the same retinal area. This area, depicted in Fig. 1, includes the optic disc and temporal vessels in the lower field. Arbitrary selection of field of view is necessary to ensure the same vessels can be measured in each photograph. The only rationale for this particular selection was that Stokoe and Turner⁶ found more comparable pairs among temporal than among nasal vessels.

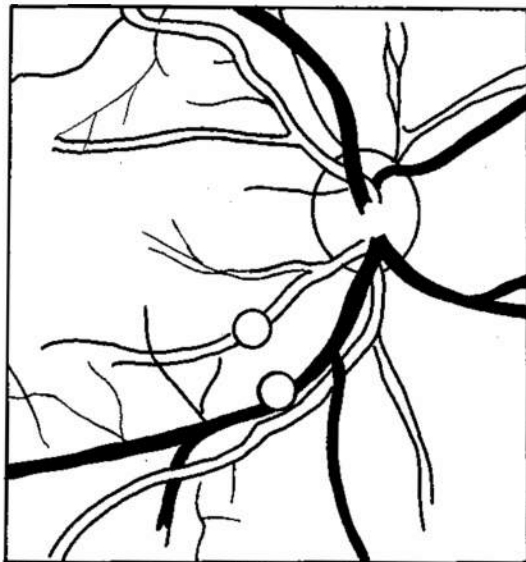


Fig. 1. The area of the retina photographed, with the positions of the arteriole and venule measures designated by ○

After the photographs are developed, the procedure of measurement consists of three steps:

(1) The slides are projected and the best photograph is selected. Clarity of

focus is extremely important for the measures; improperly focused photographs are discarded.

(2) A sketch of the configurations of vessels around the disc is made for each individual subject. The positions in which the blood vessels are to be measured are indicated on the sketch. This is necessary for the permanent record since individual patterns of blood vessels may differ considerably from the standard depicted in Fig. 1.

The desired site of measurement is at a distance of one disc diameter from the edge of the disc in the lower field. Comparable temporal vessels are to be measured if possible. The following additional instructions for designating the position on the arteriole and venule to be measured are followed:

- (a) If the vessel bifurcates at the desired measurement site, move away from the bifurcation to mark the position. The direction of movement, toward or away from the disc, is governed by the instructions to make the measured area fall in the same section, or order of branching, as that of the comparable vessel.
- (b) If the vessel bifurcates into two parts of unequal size, select the larger arteriole and venule for comparison.

- (c) If comparable vessels cannot be found, select the most temporal venule and arteriole, adhering to the same instructions as for comparable vessels.

Figure 2 illustrates the operation of the above principles in the actual selection of locations to be measured.

(3) Vessels on the slides are measured with a standard measuring microscope. Our instrument, manufactured by Central Scientific Co., consists of a 10x microscope mounted on a sliding carriage with a centimeter scale and vernier capable of precision to .01 mm.

Cross-hairs were positioned on an illuminated viewing screen; the cross-hairs in the microscope are first aligned with those on the viewing screen. The slide is then positioned with the area to be measured between the two sets of cross-hairs; this simply allows the designated area to be easily located in the magnified field of view. Measures of the caliber of the arteriole and venule are made and recorded to the nearest .01 mm and the A/V ratio calculated from them. Measures were divided by 2.5, the magnification factor of the Zeiss Ikon Camera, to obtain retinal sizes.

This technique of measuring fundus slides with a microscope and cross-hairs is very similar to that of Hodge, et al; they report it to be the most reliable of four different methods of measurement.⁹

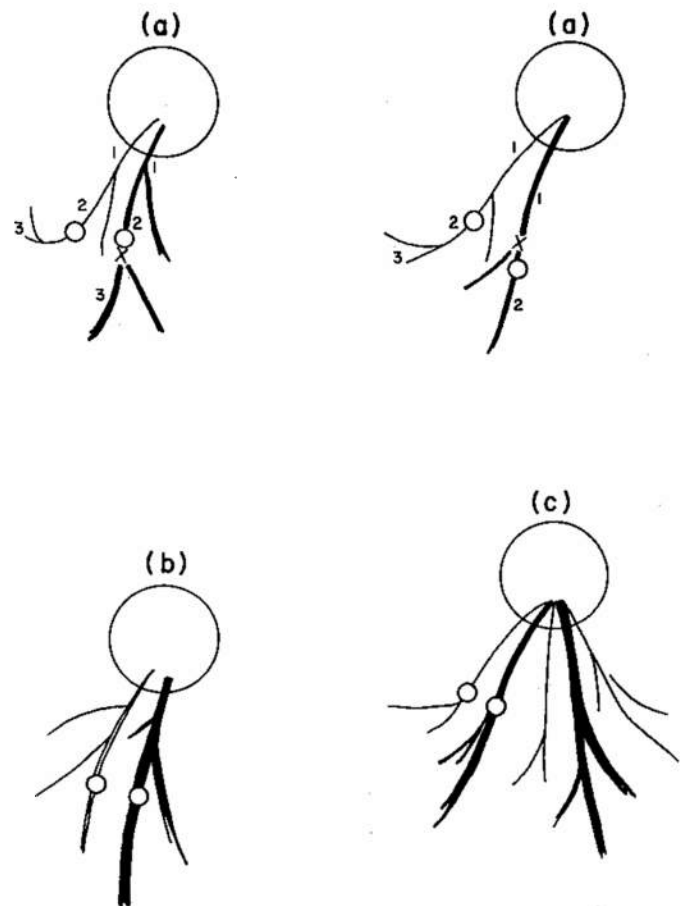


Fig. 2. Examples of special instructions for selection of sites to be measured, -- the sites designated by \bigcirc for three special circumstances:

- (a) if bifurcation comes at distance from disc where measure should be made;
 (b) if vessels bifurcate into unevenly sized branches,
 and (c) if subject does not have comparable vessels.

MEASUREMENTS

Slides have been measured for the fundi of the right eyes of 40 men following the procedures outline above. The men were all between 20 and 27 years of age with a median age of 21. Their systolic and diastolic blood pressure varied from 102 to 150 with a mean of 124 and from 66 to 90 with a mean of 76, respectively.

Table II lists the means and standard deviations of the obtained values for two different measurers. The average size of the temporal retinal arteriole at a distance of 1 disc diameter for healthy young men is 94 micra. The standard deviation of 16 micra means that 95% of the men examined have arterioles lying between 63 and 125 μ . The average size of the comparable venule is larger, 133 micra, with a similar distribution of values around it.

Arteriole/venule ratios, calculated from these values, average .71 with a standard deviation of .109. Calculations based upon the normal curve estimate

95% of these men have A/V ratios between .50 and .92; the actual range found is not very different. These A/V ratios agree well with values in the literature; 2/3 or 3/4 is the commonly accepted range. The overall mean of .71 can be compared with Nicholls et al's mean for normals of .76. The ranges of A/V ratios are also very similar to those reported by Nicholls for normal subjects (see Table I).

The degree of agreement by the two measurers, depicted in the scatter diagram of Fig. 3 and in the correlation coefficients of Table II is generally good. It is of the same order of magnitude as that found by Nicholls et al for the two highly trained ophthalmologists working under ideal conditions. 88.3% of their measures differed by .1 or less while 11.7% differed by .2 or more. Comparable values here are 82.5% differ by .1 or less; 15% between .1 and .2; and 2.5% by .2 or more.

While the error of measurement using the photographic technique is no less, two major advantages accrue:

Table II. Sample Measures of Arteriole and Venule Calibers, in Micra, of Photographs of Fundi of 40 Young, Healthy Men.

Measurer	Arteriole		Venule		A/V Ratios		Range
	Mean	σ	Mean	σ	Mean	σ	
AR	96	14	132	22	.72	.104	.52 - .97
CM	92	18	136	19	.69	.109	.48 - .91
Correlation	.79		.89		.79		

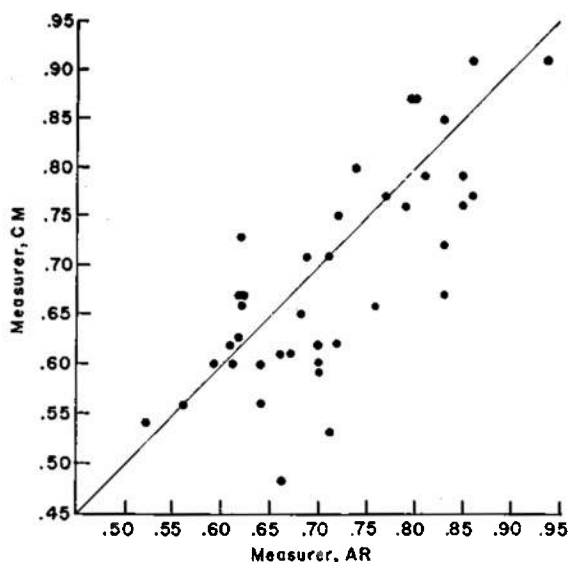


Fig. 3. Scatter diagram of the arteriole to venule ratios made on 40 men by two different measurers.

trained ophthalmologists are not required and a permanent record is available for remeasurement at any time in the future.

SUMMARY

A technique for obtaining sizes of retinal vessels and A/V ratios by measurement of fundus photography has been described. The measures are reliable and the vessel sizes are comparable to values found in the literature. The technique overcomes some of the objections that have been raised to the use of A/V ratios in assessing the health of an individual's vascular system.

Specifically, the technique provides an objective measure of retinal vessels; not only does it not require trained ophthalmologists but it can best be utilized by a practiced measurer with no knowledge of the health of the subject. Second, the method circumvents many of the problems that commonly arise in finding comparable vessels. This is considerably easier in projected slides than in a moving eye. Furthermore, if comparables do not exist, the slide is a permanent record by which future changes may be assessed; comparison of an artery's caliber with that of a vein is necessary only if no other standard is available.

Finally, the use of a standard technique and location of measurement and the amassing of data with proper measures of central tendency and variability will minimize the difficulty of prognosis for individuals. While this will not, of course, eliminate the overlap of distributions of A/V ratios of patients and normals, it will allow prediction of vascular health with known probabilities of predictive error.

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